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10/735,098	12/12/2003	Annika Margareta Pettersson-Fernholm	B45106C1	2512

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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,098	PETTERSSON-FERNHOLM ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-53* is/are pending in the application.

4a) Of the above claim(s) *40-52,54 and 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-39 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/485,760.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 35-39 and 53, in the paper filed 8/9/04 is acknowledged. The traversal is on the ground(s) that there is a technical relationship among the inventions involving one or more of the same or corresponding technical features. This is not found persuasive because the instant case is not a National Stage Application and PCT Rule 13.2 does not apply. Continuations of a National Stage application are subject to 35 U.S.C. 121, not PCT Rule 372. Groups I-III (polynucleotides, polypeptides, and antibodies) are biologically, chemically and structurally different products and, therefore, are patentably distinct and independent inventions. Applicants also argue that the sequences in Group I encode homologues of the same protein and that a reasonable number of sequences should be examined together. This has been fully and carefully considered, but is not deemed persuasive. The DNA sequences of SEQ ID NOS: 1, 3, 5, 7 and 9 were aligned and were shown to have great variability. They encode very different proteins. The search would not be coextensive. The sequence facility at the PTO estimated that the search for all of these sequences would run over 30+ hours. However, in the parent application (09/485,760), which was a 371 US National stage application, the Examiner searched all of the DNA sequences together. Accordingly, all of the SEQ ID Nos. recited in the elected Group, i.e, SEQ ID Nos: 1 (nucleotides 100-2274), 3, 5, 7 and 9 will be examined.

Claims 40-52, 54 and 55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. The requirement is still deemed proper and is therefore made **FINAL**.

Sequence Compliance

2. It is noted that Figures 3, 4 and 9 (pages 9/15 & 10/15) of the instant specification recites a nucleotide/amino acid sequence which is encompassed by the definitions for nucleotide sequences as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). The M.P.E.P., Section 2422.02, 37 CFR 1.821(b) requires exclusive conformance, with regard to the manner in which the nucleotide/amino acid sequences are presented and described, with the sequence rules for all applications that include nucleotide sequences that fall within the definitions. When a sequence is presented in a drawing, regardless of the format or the manner of the presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier (SEQ ID NO:X) must be used, either in the drawing or in the Brief Description of the Drawings. It the sequences recited in Fig. 3, 4 or 9 is in the Sequence Listing are not recited in the sequence listing- APPLICANT MUST COMPLY WITH THE SEQUENCE RULES WITHIN THE SAME TIME PERIOD AS IS GIVEN FOR RESPONSE TO THIS ACTION, 37 C.F.R. 1.821-25. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. 1.136. In no case may an applicant extend the period for response beyond the six month statutory period.

Claim Rejections - 35 USC 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 35-39 and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 is vague and indefinite because it is unclear what structure is being claimed. The claim allows for a 20% difference in the recited sequences. It is unclear what structures are encompassed by this claim. The metes and bounds of the claim cannot be understood. See 112, first enablement rejection below.

Claim 36 is vague and indefinite due to the phrase "recombinant expression system". What is encompassed by this terminology? Is this an expression vector comprising the polynucleotides of claim 35? Correction is required.

Claims 38 and 39 vague and indefinite because it is unclear how a polynucleotide sequence which varies by 20% will have the capability of producing a LbpB polypeptide. The specification is silent as to the nucleotide changes which can be made to the defined sequences and still produce a functional protein. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are

incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. See 112, first enablement rejection below.

Claim 38 should be amended to recite "A process for producing a 'host' cell" in order to clarify that it is a transformed cell which is being produced.

Claim 53 should be amended to a kit comprising an "isolated' polynucleotide".

Claim Rejections - 35 USC 112- first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 35-39 and 53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "an isolated polynucleotide encoding *Neisseria meningitidis* LbpB selected from the group consisting of: SEQ ID NO:1 (nucleotide 100-nucleotide2274), SEQ ID NO: 3, SEQ ID NO:5, SEQ ID NO:7, or SEQ ID NO:9' and for an isolated polynucleotide which encodes the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, or SEQ ID NO:10' and host cells and test kits comprising the polynucleotide sequences, does not reasonably provide enablement for "An isolated polynucleotide encoding a *Neisseria meningitidis* LbpB protein, selected from the group consisting of: an isolated polynucleotide sequence that is <u>at least 80%</u> identical to that of SEQ ID NO:1 (nucleotide 100-nucleotide2274), SEQ ID Nos: 3, 5, 7, or 9", nor is it enabled for methods of making a protein using these polynucleotides of for test kits for diagnosing

neisserial bacteria in a human which comprise these polynucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to the protein to be produced. Further, it is unpredictable as to which nucleotides could be removed and which could be added. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein' sequence where amino acid substitutions can be made with a reasonable expectation of success are limited. Other positions are critical to the protein' structure/function relationship, e.g., such as various positions or regions directly involved in binding, catalysis in providing the correct three-dimensional spatial orientation of binding and catalytic sites. These regions can tolerate only very little or no substitutions. Applicants have provides no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made.

It is well known in the prior art that selective point mutation to one key amino acid residue eliminate the ability of an antibody to recognize this altered protein. If the range of decreased binding ability after single point mutation of a protein varies one could

expect point mutations in the protein antigen to cause varying degrees of loss of function, depending on the relative importance to the binding interaction of the altered residue. Alternatively, the combined effects of multiple changes in an antigenic determinant could again result in loss of function. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool. A nucleotide sequence with 20% random difference may very well lose the ability to bind to human lactoferrin as required by the claims and is unlikely to produce a functional LbpB polypeptide as required by claims 36-39. Additionally, a polynucleotide sequence with a 20% difference will not function as a reliable detection agent in a kit for diagnosing infection with neisserial bacteria. To start with the DNA sequence first, this requires even more work on the part of the skilled artisan.

Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. Given the lack of guidance contained in the specification and the unpredictability for determining acceptable nucleotide substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Claim Rejections - 35 USC 112-Written Description

7. Claims 35-39 and 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:1(from nucleotide 100 to nucleotide 2274), 3, 5, 7 and 9 and equivalent degenerative codon sequences thereof, i.e., isolated polynucleotides encoding the amino acid sequence set forth in SEQ ID Nos: 2, 4, 6, 8 or 10, and therefore the written description is not commensurate in scope with the claims which are broadly drawn to any isolated polynucleotide encoding N.meningitidis LbpB (claim35) and polynucleotides which vary by 20% of the known sequences.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID Nos:1 (from nucleotide 100 to nucleotide 2274), 3, 5, 7, and 9 and

the degenerates thereof, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

However, no disclosure, beyond the mere mention of allelic variants is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated polynucleotide comprising SEQ ID NO:1 (from nucleotide 100 to nucleotide 2274), 3, 5, 7 and 9 and equivalent degenerative codon sequences thereof, i.e., isolated polynucleotides encoding the amino acid sequence set forth in SEQ ID Nos: 2, 4, 6, 8 or 10, but not the full breadth of the claims meets the written description provisions of 35 USC 112, first paragraph.

Allowable Subject Matter

8. An isolated polynucleotide consisting of SEQ ID Nos: 1 (from nucleotide 100 to nucleotide 2274), 3, 5, 7 or 9 is free of the prior art.

9. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 872-9306 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

Jennifer Graser
Primary Examiner
Art Unit 1645

9/1/04